Heritage Information Systems, Inc.

SmartPA

Step-Therapy Criteria Proposal

Drug/Drug Class: COX-2 Inhibitors

Prepared for: Missouri Medicaid

Prepared by: Heritage Information Systems, Inc.

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose: Reduce drug costs by decreasing use of COX-2 inhibitors in patients without indications for use. Also, reduce the potential for adverse events associated with chronic, high dose rofecoxib use.

Why was this Issue Selected: For the previous reporting period (August 2001 – July 2002), Missouri Medicaid paid $28.4 million for COX-2 inhibitors. This represents 3.6% of the total drug budget.

Program-specific information:

Performance Indicator	Exceptions	Candidates
Use of COX-2 inhibitors in the absence of risk factors for GI toxicity	*7,789*	*41,611*

Setting & Population: All individuals ≥12 years of age receiving a COX-2 inhibitor.

Type of Criteria:
☒ **Increased risk of ADE**
☒ **Appropriate Indications**
☐ **Non-Preferred Agent**
☐

Data Sources: ☐ **Only administrative databases** ☐ **Databases + Prescriber-supplied**

Purpose of PA Criteria

Prior authorization criteria assist in the achievement of economic and qualitative goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class. Prior authorization criteria can also reduce the risk for adverse events associated with medications by identifying patients at increased risk due to diseases or medical conditions, or those in need of dosing modifications.

Why Has This Clinical Issue Been Selected For Review?

NSAIDs are one of the most commonly prescribed classes of drugs.[1] COX-2 inhibitors are members of the NSAID drug class, but differ in their selectivity for the COX-2 isoenzyme. Three selective COX-2 inhibitors (also known as COX-1 sparing agents) are currently available in the United States: celecoxib (Celebrex®), rofecoxib (Vioxx®) and valdecoxib (Bextra®). All three agents have FDA approved indications for the treatment of osteoarthritis, rheumatoid arthritis in adults, and primary dysmenorrhea. Additionally, celecoxib and rofecoxib have indications for the treatment of acute pain, and celecoxib is approved for the reduction of adenomatous colorectal polyps in patients with familial adenomatous polyposis (FAP). Market share of these agents within the NSAID drug class has steadily increased since their introduction to the market in early 1999. The selective COX-2 inhibitors were developed in an effort to reduce the GI toxicity associated with NSAIDs. Gastrointestinal (GI) problems are the most common side effects associated with NSAID use. Approximately 15% of NSAID users will have dyspepsia and 1-4% will have significant GI complications each year (e.g., perforated ulcers or GI bleeding requiring hospitalization).[2] Selective COX-2 inhibitors show similar analgesic and anti-inflammatory efficacy as traditional non-selective NSAIDs, but with significantly reduced rates of serious GI complications.[3,4] The American Pain Society recently published guidelines for the management of arthritis pain in which COX-2 inhibitors are promoted as first-line therapy over nonselective NSAIDs.[5] However, the COX-2 inhibitors are significantly more expensive than generic non-selective NSAIDs and their use in patients without risk factors for NSAID-induced GI toxicity may not be cost-effective.[6] The decision to use a COX-2 inhibitor should largely be influenced by the potential to improve the safety profile in patients at risk for gastrointestinal (GI) toxicity.

The following factors have been identified as placing NSAID-using patients at greater risk for GI adverse events:[7,8]

- Advanced age (defined as >65-75 years old by most studies)
- High dose NSAID use
- Concurrent use of NSAIDs and corticosteroids
- Concurrent use of NSAIDs and oral anticoagulants
- Prior history of GI events (e.g., GI hemorrhage or ulcer)

Smoking and alcohol use have been reported to increase the risk of NSAID-induced ulcers, but the reported relationships between these factors are inconsistent. Use of multiple NSAIDs has also been reported to increase the risk of adverse GI events, as well as serious underlying disease.

While COX-2 inhibitors reduce the risk of GI toxicity, they share the potential risks for adverse renal effects with the nonselective NSAIDs. Additionally, concerns over adverse cardiovascular effects of rofecoxib were raised recently upon publication of the VIGOR trial.[3] An increased incidence of cardiovascular thrombotic events in rofecoxib patients was observed as compared to patients receiving naproxen. Whether this difference was due to an increased risk conferred by rofecoxib, or a protective effect conferred by naproxen, or a combination of both, is unclear. The makers of rofecoxib recently added language to the Vioxx® product labeling indicating that the dose of 50 mg should not be used chronically due to the risk for serious adverse events, including lower extremity edema and increased blood pressure.[9] Therefore, while the COX-2 inhibitors have potential GI benefits over nonselective NSAIDs, they are not without risks of themselves.

Setting & Population

- **Drug class for review: COX-2 inhibitors**
- **Age range: Age < 12 not reviewed**

Approval Criteria

Approval Diagnoses			
Condition	**Submitted ICD-9 Diagnoses**	**Inferred Drugs**	**Date Range**
Familial adenomatous polyposis* (Celecoxib only)	• Familial adenomatous polyposis	N/A	2 years
GI toxicity risk factors*	• Age ≥65 • PUD or GI bleed	N/A N/A • warfarin • corticosteroids • high-dose NSAID	N/A 2 years 45 days 90 days* 45 days
Arthritis*	• Rheumatoid arthritis • Osteoarthritis	N/A N/A • DMARDs	2 years 2 years 45 days
Significant other comorbidity* (discretion of call-center staff)	N/A	N/A	N/A
Therapeutic failure*	N/A	• NSAIDs (≥2)	6 months

*Approved for up to1 year

Denial Criteria

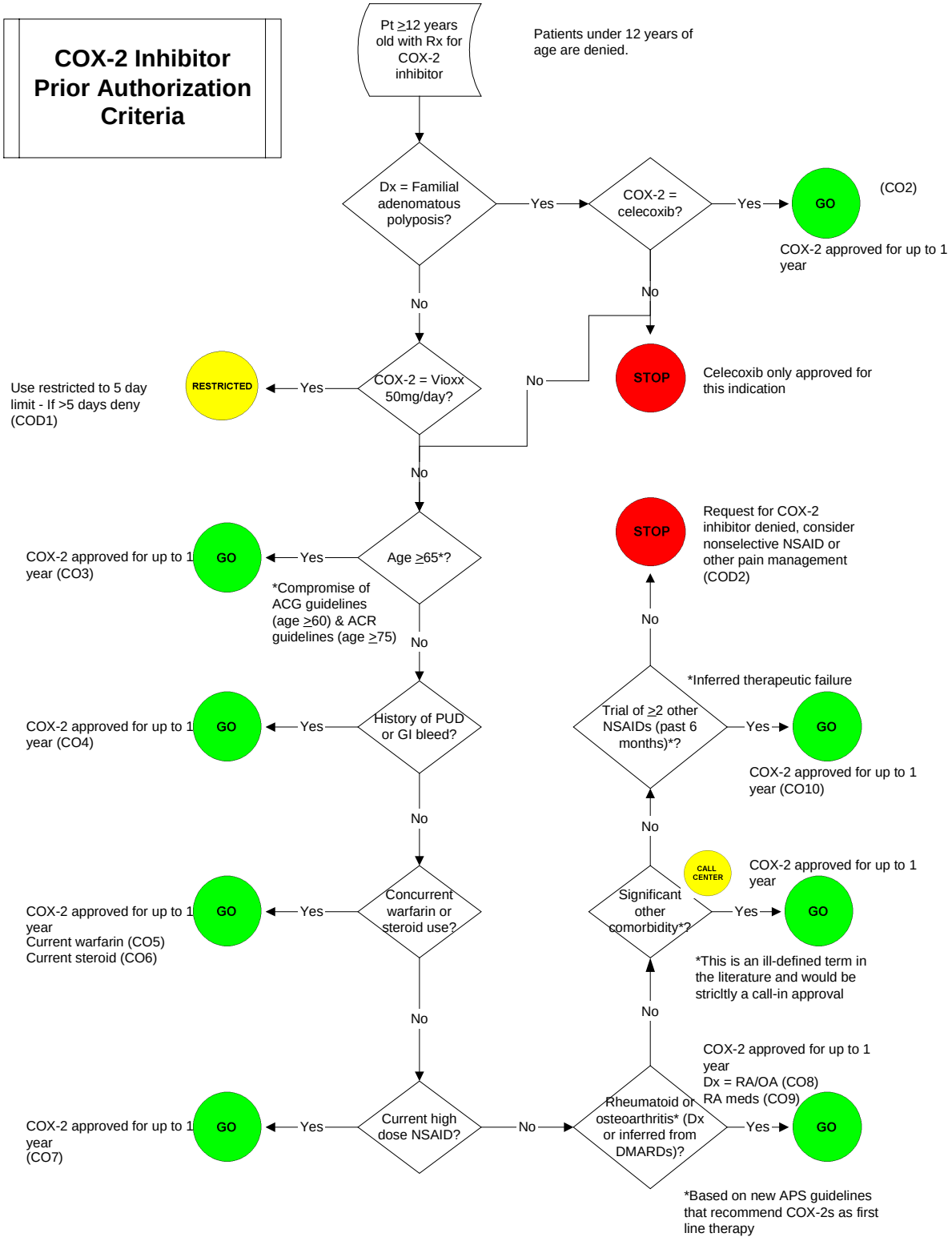
Requests for COX-2 therapy will denied in the absence of approval criteria and under the following condition:

- Patients with a diagnosis of familial adenomatous polyposis presenting with a prescription for a COX-2 inhibitor other than celecoxib. (Celecoxib only approved for this indication.)

Required Documentation

- Laboratory results
- MedWatch form
- Progress notes

Flowchart of Criteria



References

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